* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 12:23:49 ON 27 AUG 2007

=> **file registry**

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 12:24:10 ON 27 AUG 2007


Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 26 AUG 2007 HIGHEST RN 945604-45-5
DICTIONARY FILE UPDATES: 26 AUG 2007 HIGHEST RN 945604-45-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

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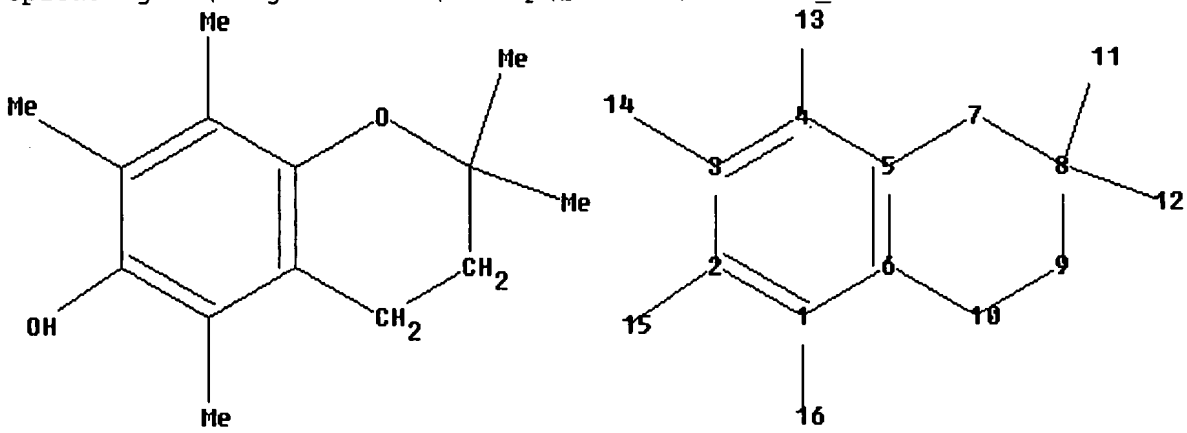
Uploading C:\Program Files\Stnexp\Queries\10789835_NEW.str



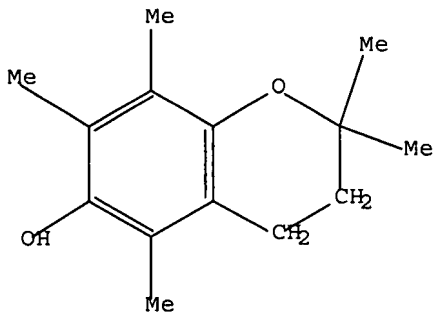

chain nodes :
11 12 13 14 15 16
ring nodes :
1 2 3 4 5 6 7 8 9 10
chain bonds :
1-16 2-15 3-14 4-13 8-11 8-12
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10

exact/norm bonds :
2-15  5-7  6-10  7-8  8-9  9-10
exact bonds :
1-16  3-14  4-13  8-11  8-12
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:CLASS  12:CLASS  13:CLASS  14:CLASS  15:CLASS  16:CLASS

L1  STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1  STR




Structure attributes must be viewed using STN Express query preparation.

=> **s l1 exa full**
FULL SEARCH INITIATED 12:24:28 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  68 TO ITERATE

100.0% PROCESSED  68 ITERATIONS  8 ANSWERS
SEARCH TIME: 00.00.01

L2  8 SEA EXA FUL L1

=> **file medline, caplus, wpids, uspatfull**
COST IN U.S. DOLLARS  SINCE FILE ENTRY  TOTAL SESSION
FULL ESTIMATED COST  58.25  58.46

FILE 'MEDLINE' ENTERED AT 12:24:41 ON 27 AUG 2007

FILE 'CAPLUS' ENTERED AT 12:24:41 ON 27 AUG 2007

FILE 'WPIDS' ENTERED AT 12:24:41 ON 27 AUG 2007
COPYRIGHT (C) 2007 THE THOMSON CORPORATION

FILE 'USPATFULL' ENTERED AT 12:24:41 ON 27 AUG 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

=> s l2
SAMPLE SEARCH INITIATED 12:24:45 FILE 'WPIDS'
SAMPLE SCREEN SEARCH COMPLETED - 62 TO ITERATE

100.0% PROCESSED 62 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 384 TO 856
PROJECTED ANSWERS: 0 TO 0

L3 511 L2

=> **s l3 and "prostate cancer"**
2 FILES SEARCHED...
L4 11 L3 AND "PROSTATE CANCER"

=> **d l4 1-11 ibib, abs, hitstr**

L4 ANSWER 1 OF 11 MEDLINE on STN
ACCESSION NUMBER: 2003400986 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12939470
TITLE: Androgen antagonist activity by the antioxidant moiety of vitamin E, 2,2,5,7,8-pentamethyl-6-chromanol in human prostate carcinoma cells.
AUTHOR: Thompson Todd A; Wilding George
CORPORATE SOURCE: University of Wisconsin Comprehensive Cancer Center, University of Wisconsin-Madison, Madison, Wisconsin 53792, USA.
SOURCE: Molecular cancer therapeutics, (2003 Aug) Vol. 2, No. 8, pp. 797-803.
Journal code: 101132535. ISSN: 1535-7163.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 27 Aug 2003
Last Updated on STN: 24 Jun 2004
Entered Medline: 21 Jun 2004

AB Antioxidants, such as vitamin E, are being investigated for efficacy in prostate cancer prevention. In this study, we show that the antioxidant moiety of vitamin E, 2,2,5,7,8-pentamethyl-6-chromanol (PMCol), has antiandrogen activity in prostate carcinoma cells. In the presence of PMCol, the androgen-stimulated biphasic growth curve of LNCaP human prostate carcinoma cells was shifted to the right. The PMCol-induced growth shift was similar to that produced by treatment with the pure antiandrogen bicalutamide (i.e., Casodex), indicative of androgen receptor (AR) antagonist activity. The concentration of PMCol used was below the concentration required to affect cell growth or viability in the absence of androgen. Using an AR binding competition assay, PMCol was found to be a potent antiandrogen in both LNCaP

and LAPC4 cells, with an IC(50) of approximately 10 micro M against 1 nM R1881 (methyltrienolone; a stable, synthetic androgen). Prostate-specific antigen release from LNCaP cells produced by androgen exposure with either 0.05 or 1.0 nM R1881 was inhibited 100% and 80%, respectively, by 30 micro M PMCol. Also, PMCol inhibited androgen-induced promoter activation in both LNCaP and LAPC4 cells. However, PMCol did not affect AR protein levels, suggesting that the inhibitory effects of PMCol on androgenic pathways were not due to decreased expression of the AR. Therefore, growth modulation by the antioxidant moiety of vitamin E in androgen-sensitive prostate carcinoma cells is due, at least in part, to its potent antiandrogenic activity.

L4 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:120717 CAPLUS Full-text
DOCUMENT NUMBER: 142:170094
TITLE: Chroman-derived antiandrogens for treatment of androgen-mediated disorders
INVENTOR(S): Thompson, Todd A.; Wilding, George
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005011658 | A2 | 20050210 | WO 2004-US5872 | 20040227 |
| WO 2005011658 | A3 | 20050519 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004260631 | A1 | 20050210 | AU 2004-260631 | 20040227 |
| CA 2517390 | A1 | 20050210 | CA 2004-2517390 | 20040227 |
| US 2005192342 | A1 | 20050901 | US 2004-789835 | 20040227 |
| EP 1596857 | A2 | 20051123 | EP 2004-785845 | 20040227 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |

PRIORITY APPLN. INFO.: US 2003-450510P P 20030227
WO 2004-US5872 A 20040227

OTHER SOURCE(S): MARPAT 142:170094

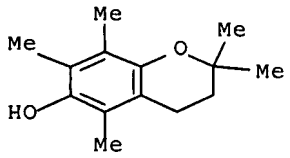
AB Methods for the prevention and/or alleviation of androgen-mediated disorders treatable by administering a chroman-derived antiandrogen compound are provided by the invention. The invention further provides pharmaceutical and nutraceutical compns. containing chroman-derived antiandrogen compds. useful in the prevention and/or alleviation of androgen-mediated disorders, particularly prostate cancer. Compds. of the invention include e.g. 2,2,5,7,8-pentamethyl-6-chromanol.

IT 950-99-2, 2,2,5,7,8-Pentamethyl-6-chromanol
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(chroman-derived antiandrogens for treatment of androgen-mediated disorders)

RN 950-99-2 CAPLUS

CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L4 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:665773 CAPLUS Full-text

DOCUMENT NUMBER: 140:52950

TITLE: Androgen Antagonist Activity by the Antioxidant Moiety of Vitamin E, 2,2,5,7,8-Pentamethyl-6-chromanol in Human Prostate Carcinoma Cells

AUTHOR(S): Thompson, Todd A.; Wilding, George

CORPORATE SOURCE: University of Wisconsin Comprehensive Cancer Center and University of Wisconsin Department of Medicine, University of Wisconsin-Madison, Madison, WI, 53792, USA

SOURCE: Molecular Cancer Therapeutics (2003), 2(8), 797-803
CODEN: MCTOCF; ISSN: 1535-7163

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

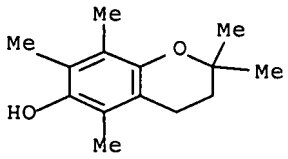
LANGUAGE: English

AB Antioxidants, such as vitamin E, are being investigated for efficacy in prostate cancer prevention. In this study, we show that the antioxidant moiety of vitamin E, 2,2,5,7,8-pentamethyl-6-chromanol (PMCol), has antiandrogen activity in prostate carcinoma cells. In the presence of PMCol, the androgen-stimulated biphasic growth curve of LNCaP human prostate carcinoma cells was shifted to the right. The PMCol-induced growth shift was similar to that produced by treatment with the pure antiandrogen bicalutamide (i.e., Casodex), indicative of androgen receptor (AR) antagonist activity. The concentration of PMCol used was below the concentration required to affect cell growth or viability in the absence of androgen. Using an AR binding competition assay, PMCol was found to be a potent antiandrogen in both LNCaP and LAPC4 cells, with an IC50 of approx. 10 μM against 1 nM R1881 (methyltrienolone; a stable, synthetic androgen). Prostate-specific antigen release from LNCaP cells produced by androgen exposure with either 0.05 or 1.0 nM R1881 was inhibited 100% and 80%, resp., by 30 μM PMCol. Also, PMCol inhibited androgen-induced promoter activation in both LNCaP and LAPC4 cells. However, PMCol did not affect AR protein levels, suggesting that the inhibitory effects of PMCol on androgenic pathways were not due to decreased expression of the AR. Therefore, growth modulation by the antioxidant moiety of vitamin E in androgen-sensitive prostate carcinoma cells is due, at least in part, to its potent antiandrogenic activity.

IT 950-99-2, 2,2,5,7,8-Pentamethyl-6-chromanol
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(androgen antagonist activity by the antioxidant moiety of vitamin E, 2,2,5,7,8-pentamethyl-6-chromanol in human prostate carcinoma cells)

RN 950-99-2 CAPLUS

CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 11 USPATFULL on STN

| | | | | |
|---|---|---|---|---|
| ACCESSION NUMBER: | 2006:27860 USPATFULL Full-text | | | |
| TITLE: | Novel pathways in the etiology of cancer | | | |
| INVENTOR(S): | Benz, Christopher C., Novato, CA, UNITED STATES | | | |
| PATENT ASSIGNEE(S): | Buck Institute for Age Research (U.S. corporation) | | | |

| | NUMBER | KIND | DATE | |
|---|---|---|---|---|
| PATENT INFORMATION: | US 2006024691 | A1 | 20060202 | |
| APPLICATION INFO.: | US 2005-90546 | A1 | 20050324 | (11) |

| | NUMBER | DATE | |
|---|---|---|---|
| PRIORITY INFORMATION: | US 2004-556774P | 20040325 | (60) |
| | US 2004-580534P | 20040616 | (60) |
| | US 2004-629691P | 20041119 | (60) |

| | |
|---|---|
| DOCUMENT TYPE: | Utility |
| FILE SEGMENT: | APPLICATION |
| LEGAL REPRESENTATIVE: | QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C., P O BOX 458, ALAMEDA, CA, 94501, US |
| NUMBER OF CLAIMS: | 30 |
| EXEMPLARY CLAIM: | 1 |
| NUMBER OF DRAWINGS: | 19 Drawing Page(s) |
| LINE COUNT: | 2824 |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

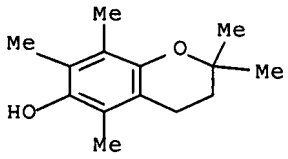
AB This invention pertains to the identification of two novel epithelial signaling pathways in ER-positive breast cancer s and the discovery that the cellular biology and (likely also the clinical outcome) of ER-positive breast cancer cells is unexpectedly altered when these signaling pathways are activated. The first pathway pertains to the discovery that NF-κB activation and/or DNA binding is implicated in the etiology of ER-positive breast (and other) cancers. The second pathway involves ligand-independent quinine-mediated ER activation by posphorylation (e.g. on SER-118 and SER-167 residues of ER) and nuclear translocation of full-length (67 kDA) ER as well as the phorphorylating activation of a truncated and nuclear-localized ER variant (.about.52 kDa).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 950-99-2
(pathways in etiol. of cancer, and treatment methods)

RN 950-99-2 USPATFULL

CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)



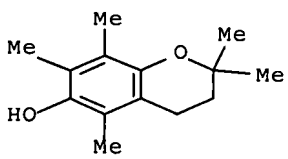
L4 ANSWER 5 OF 11 USPATFULL on STN
ACCESSION NUMBER: 2005:221605 USPATFULL Full-text
TITLE: Chroman-derived anti-androgens for treatment of androgen-mediated disorders
INVENTOR(S): Thompson, Todd A., Madison, WI, UNITED STATES
Wilding, George, Verona, WI, UNITED STATES
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation (U.S. corporation)

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2005192342 | A1 | 20050901 |
| APPLICATION INFO.: | US 2004-789835 | A1 | 20040227 (10) |

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 2003-450510P | 20030227 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: GODFREY & KAHN, S.C., 780 N. WATER STREET, MILWAUKEE, WI, 53202, US
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Page(s)
LINE COUNT: 1654
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the prevention and/or alleviation of androgen-mediated disorders treatable by administering a chroman-derived anti-androgen compound are provided by the present invention. The invention further provides pharmaceutical and nutraceutical compositions containing chroman-derived anti-androgen compounds useful in the prevention and/or alleviation of androgen-mediated disorders, particularly prostate cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 950-99-2, 2,2,5,7,8-Pentamethyl-6-chromanol
(chroman-derived antiandrogens for treatment of androgen-mediated disorders)
RN 950-99-2 USPATFULL
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)



L4 ANSWER 6 OF 11 USPATFULL on STN

ACCESSION NUMBER: 2004:300069 USPATFULL Full-text

TITLE: Tocopherols, tocotrienols, other chroman and side chain derivatives and uses thereof

INVENTOR(S): Sanders, Bob G., Austin, TX, UNITED STATES
Kline, Kimberly, Austin, TX, UNITED STATES
Hurley, Laurence, Austin, TX, UNITED STATES
Gardner, Robb, Austin, TX, UNITED STATES
Menchaca, Marla, Austin, TX, UNITED STATES
Yu, Weiping, Austin, TX, UNITED STATES
Ramanan, Puthucode N., Austin, TX, UNITED STATES
Liu, Shenquan, Austin, TX, UNITED STATES
Israel, Karen, Austin, TX, UNITED STATES

PATENT ASSIGNEE(S): Research Development Foundation (U.S. corporation)

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2004235938 | A1 | 20041125 |
| APPLICATION INFO.: | US 2003-644418 | A1 | 20030820 (10) |

RELATED APPLN. INFO.: Division of Ser. No. US 2000-502592, filed on 11 Feb 2000, GRANTED, Pat. No. US 6770672 Continuation-in-part of Ser. No. US 1999-404001, filed on 23 Sep 1999, GRANTED, Pat. No. US 6417223

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1998-101542P | 19980923 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Benjamin Aaron Adler, ADLER & ASSOCIATES, 8011 Candle Lane, Houston, TX, 77071
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 21 Drawing Page(s)
LINE COUNT: 2556

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides an antiproliferative compound having the structural formula ##STR1##

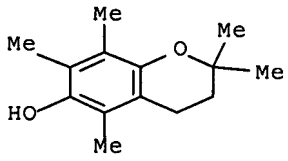
wherein X is oxygen, nitrogen or sulfur; Y is selected from the group consisting of oxygen, nitrogen and sulfur wherein when Y is oxygen or nitrogen, n is 1 and when Y is sulfur, n is 0. Also provided is a method for inducing apoptosis in a cell comprising administering a composition comprising a compound.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 950-99-2
(preparation of tocopherols, tocotrienols, other chroman and side chain derivs. for use as antitumor agents and for inducing cell apoptosis)

RN 950-99-2 USPATFULL

CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L4 ANSWER 7 OF 11 USPATFULL on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2004:192666 USPATFULL Full-text |
| TITLE: | Tocopherols, tocotrienols, other chroman and side chain derivatives and uses thereof |
| INVENTOR(S): | Sanders, Bob G., Austin, TX, United States<br>Kline, Kimberly, Austin, TX, United States<br>Hurley, Laurence, Austin, TX, United States<br>Gardner, Robb, Austin, TX, United States<br>Menchaca, Marla, Austin, TX, United States<br>Yu, Weiping, Austin, TX, United States<br>Ramanan, Puthucode N., Austin, TX, United States<br>Liu, Shenquan, Austin, TX, United States<br>Israel, Karen, Austin, TX, United States |
| PATENT ASSIGNEE(S): | Research Development Foundation, Carson City, NV, United States (U.S. corporation) |

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 6770672 | B1 | 20040803 |
| APPLICATION INFO.: | US 2000-502592 | | 20000211 (9) |

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1999-404001, filed on 23 Sep 1999, now patented, Pat. No. US 6417223, issued on 9 Jul 2002

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1998-101543P | 19980923 (60) |

| | |
|---|---|
| DOCUMENT TYPE: | Utility |
| FILE SEGMENT: | GRANTED |
| PRIMARY EXAMINER: | Fonda, Kathleen K. |
| ASSISTANT EXAMINER: | Maier, Leigh C. |
| LEGAL REPRESENTATIVE: | Adler, Benjamin Aaron |
| NUMBER OF CLAIMS: | 4 |
| EXEMPLARY CLAIM: | 1 |
| NUMBER OF DRAWINGS: | 18 Drawing Figure(s); 21 Drawing Page(s) |
| LINE COUNT: | 2359 |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides an antiproliferative compound having the structural formula ##STR1##

wherein X is oxygen, nitrogen or sulfur; Y is selected from the group consisting of oxygen, nitrogen and sulfur wherein when Y is oxygen or nitrogen, n is 1 and when Y is sulfur, n is 0. Also provided is a method for inducing apoptosis in a cell comprising administering a composition comprising a compound.

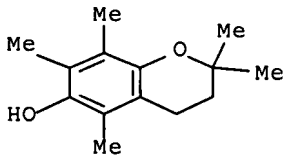
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 950-99-2, 2,2,5,7,8-Pentamethyl-6-chromanol

(preparation of tocopherols, tocotrienols, other chroman and side chain derivs. for therapeutic use in prevention and treatment of cancer)

RN 950-99-2 USPATFULL

CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L4 ANSWER 8 OF 11 USPATFULL on STN

ACCESSION NUMBER: 2004:127448 USPATFULL Full-text

TITLE: Tocopherols, tocotrienols, other chroman and side chain derivatives and uses thereof

INVENTOR(S): Sanders, Bob G., Austin, TX, UNITED STATES
Kline, Kimberly, Austin, TX, UNITED STATES
Yu, Weiping, Austin, TX, UNITED STATES

PATENT ASSIGNEE(S): Research Development Foundation (U.S. corporation)

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2004097431 | A1 | 20040520 |
| APPLICATION INFO.: | US 2003-695275 | A1 | 20031028 (10) |

RELATED APPLN. INFO.: Division of Ser. No. US 2001-8066, filed on 5 Nov 2001, GRANTED, Pat. No. US 6703384 Continuation-in-part of Ser. No. US 2000-502592, filed on 11 Feb 2000, PENDING Continuation-in-part of Ser. No. US 1999-404001, filed on 23 Sep 1999, GRANTED, Pat. No. US 6417223

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1998-101542P | 19980923 (60) |

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Benjamin Aaron Adler, Ph.D., J.D., Adler & Associates, 8011 Candle Lane, Houston, TX, 77071

NUMBER OF CLAIMS: 17

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 11 Drawing Page(s)

LINE COUNT: 2605

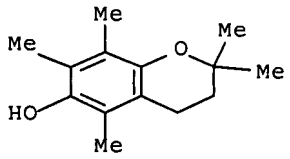
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides an antiproliferative compound having a structural formula ##STR1##

where X and Y independently are oxygen, nitrogen or sulfur; R.sup.1 is alkyl, alkenyl, alkynyl, aryl, heteroaryl, carboxylic acid, carboxylate, carboxamide, ester, thioamide, thiolacid, thiolester, saccharide, alkoxy-linked saccharide, amine, sulfonate, sulfate, phosphate, alcohol, ethers or nitrites; R.sup.2 and R.sup.3 are hydrogen or R.sup.4; R.sup.4 is methyl, benzyl carboxylic acid, benzyl carboxylate, benzyl carboxamide, benzylester, saccharide or amine; and R.sup.5 is alkenyl; where when Y is nitrogen, said nitrogen is substituted with R.sup.6, wherein R.sup.6 is hydrogen or methyl. Also provided are methods for treating a cell proliferative disease and for

inducing apoptosis in a cell comprising administering this compound is also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 950-99-2
(preparation of tocopherols, tocotrienols, other chroman and side chain derivs. for use as antitumor agents and for inducing cell apoptosis)
RN 950-99-2 USPATFULL
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L4 ANSWER 9 OF 11 USPATFULL on STN
ACCESSION NUMBER: 2002:280579 USPATFULL Full-text
TITLE: Tocopherols, tocotrienols, other chroman and side chain derivatives and uses thereof
INVENTOR(S): Sanders, Bob G., Austin, TX, UNITED STATES
Kline, Kimberly, Austin, TX, UNITED STATES
Hurley, Laurence, Austin, TX, UNITED STATES
Gardner, Robb, Austin, TX, UNITED STATES
Menchaca, Marla, Austin, TX, UNITED STATES
Yu, Weiping, Austin, TX, UNITED STATES
Ramanan, Puthucode N., Austin, TX, UNITED STATES
Liu, Shenquan, Austin, TX, UNITED STATES
Israel, Karen, Austin, TX, UNITED STATES
PATENT ASSIGNEE(S): Research Development Foundation (U.S. corporation)

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2002156024 | A1 | 20021024 |
| | US 6645998 | B2 | 20031111 |
| APPLICATION INFO.: | US 2002-122019 | A1 | 20020412 (10) |

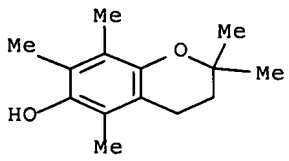
RELATED APPLN. INFO.: Division of Ser. No. US 1999-404001, filed on 23 Sep 1999, GRANTED, Pat. No. US 6417223

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1998-101542P | 19980923 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Benjamin Aaron Adler, ADLER & ASSOCIATES, 8011 Candle Lane, Houston, TX, 77071
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 14 Drawing Page(s)
LINE COUNT: 2170
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides an antiproliferative compound having the structural formula ##STR1##

wherein X is oxygen, nitrogen or sulfur; R.sup.1 is alkyl, alkenyl, alkynyl, aryl, heteroaryl, carboxylic acid, carboxylate, carboxamide, ester, thioamide, thiolacid, thiolester, saccharide, alkoxy-linked saccharide, amine, sulfonate, sulfate, phosphate, alcohol, ethers and nitriles; R.sup.2 is hydrogen, methyl, benzyl carboxylic acid, benzyl carboxylate, benzyl carboxamide, benzylester, saccharide and amine; R.sup.3 is selected from the group consisting of hydrogen, methyl, benzyl carboxylic acid, benzyl carboxylate, benzyl carboxamide, benzylester, saccharide and amine; R.sup.4 is of methyl, benzyl carboxylic acid, benzyl carboxylate, benzyl carboxamide, benzylester, saccharide and amine; and R.sup.5 is alkyl, alkenyl, alkynyl, aryl, heteroaryl, carboxyl, amide and ester. Also provided is a method for inducing apoptosis in a cell comprising administering a composition comprising a compound.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 950-99-2
(preparation of tocopherols, tocotrienols, other chroman and side chain derivs. for use as antitumor agents and for inducing cell apoptosis)
RN 950-99-2 USPATFULL
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L4 ANSWER 10 OF 11 USPATFULL on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2002:199098 USPATFULL Full-text |
| TITLE: | Tocopherols, tocotrienols, other chroman and side chain derivatives and uses thereof |
| INVENTOR(S): | Sanders, Bob G., Austin, TX, UNITED STATES<br>Kline, Kimberly, Austin, TX, UNITED STATES<br>Yu, Weiping, Austin, TX, UNITED STATES |

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2002107207 | A1 | 20020808 |
| | US 6703384 | B2 | 20040309 |
| APPLICATION INFO.: | US 2001-8066 | A1 | 20011105 (10) |

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2000-502592, filed on 11 Feb 2000, PENDING Continuation-in-part of Ser. No. US 1999-404001, filed on 23 Sep 1999, PENDING

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1998-101542P | 19980923 (60) |

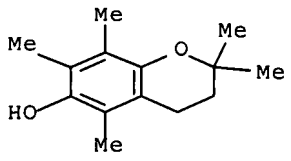
| | |
|---|---|
| DOCUMENT TYPE: | Utility |
| FILE SEGMENT: | APPLICATION |
| LEGAL REPRESENTATIVE: | Benjamin Aaron Adler, ADLER & ASSOCIATES, 8011 Candle Lane, Houston, TX, 77071 |
| NUMBER OF CLAIMS: | 24 |
| EXEMPLARY CLAIM: | 1 |

NUMBER OF DRAWINGS: 12 Drawing Page(s)
LINE COUNT: 2606
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides an antiproliferative compound having a structural formula ##STR1##

where X and Y independently are oxygen, nitrogen or sulfur; R.sup.1 is alkyl, alkenyl, alkynyl, aryl, heteroaryl, carboxylic acid, carboxylate, carboxamide, ester, thioamide, thiolacid, thiolester, saccharide, alkoxy-linked saccharide, amine, sulfonate, sulfate, phosphate, alcohol, ethers or nitrites; R.sup.2 and R.sup.3 are hydrogen or R.sup.4; R.sup.4 is methyl, benzyl carboxylic acid, benzyl carboxylate, benzyl carboxamide, benzylester, saccharide or amine; and R.sup.5 is alkenyl; where when Y is nitrogen, said nitrogen is substituted with R.sup.6, wherein R.sup.6 is hydrogen or methyl. Also provided are methods for treating a cell proliferative disease and for inducing apoptosis in a cell comprising administering this compound is also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 950-99-2, 2,2,5,7,8-Pentamethyl-6-chromanol
(preparation of tocopherols, tocotrienols, other chromans and side chain derivs. as potential antiproliferative, proapoptotic agents for the treatment of cancer)
RN 950-99-2 USPATFULL
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L4 ANSWER 11 OF 11 USPATFULL on STN
ACCESSION NUMBER: 2002:168253 USPATFULL Full-text
TITLE: Tocopherols, tocotrienols, other chroman and side chain derivatives and uses therof
INVENTOR(S): Sanders, Bob G., Austin, TX, United States
Kline, Kimberly, Austin, TX, United States
Hurley, Laurence, Austin, TX, United States
Gardner, Robb, Austin, TX, United States
Menchaca, Marla, Austin, TX, United States
Yu, Weiping, Austin, TX, United States
Ramanan, Puthucode N., Austin, TX, United States
Liu, Shenquan, Austin, TX, United States
Israel, Karen, Austin, TX, United States
PATENT ASSIGNEE(S): Research Development Foundation, Carson City, NV, United States (U.S. corporation)

| | NUMBER | KIND | DATE | |
|---|---|---|---|---|
| PATENT INFORMATION: | US 6417223 | B1 | 20020709 | |
| APPLICATION INFO.: | US 1999-404001 | | 19990923 | (9) |

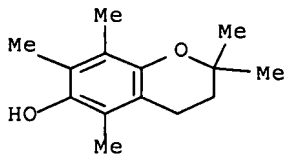
| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1998-101542P | 19980923 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Wilson, James O.
ASSISTANT EXAMINER: Maier, Leigh C.
LEGAL REPRESENTATIVE: Adler, Benjamin Aaron
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 14 Drawing Figure(s); 14 Drawing Page(s)
LINE COUNT: 1959
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides an antiproliferative compound having the structural formula ##STR1##

wherein X is oxygen, nitrogen or sulfur; R.sup.1 is alkyl, alkenyl, alkynyl, aryl, heteroaryl, carboxylic acid, carboxylate, carboxamide, ester, thioamide, thiolacid, thiolester, saccharide, alkoxy-linked saccharide, amine, sulfonate, sulfate, phosphate, alcohol, ethers and nitriles; R.sup.2 is hydrogen, methyl, benzyl carboxylic acid, benzyl carboxylate, benzyl carboxamide, benzylester, saccharide and amine; R.sup.3 is selected from the group consisting of hydrogen, methyl, benzyl carboxylic acid, benzyl carboxylate, benzyl carboxamide, benzylester, saccharide and amine; R.sup.4 is of methyl, benzyl carboxylic acid, benzyl carboxylate, benzyl carboxamide, benzylester, saccharide and amine; and R.sup.5 is alkyl, alkenyl, alkynyl, aryl, heteroaryl, carboxyl, amide and ester. Also provided is a method for inducing apoptosis in a cell comprising administering a composition comprising a compound.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 950-99-2
(preparation of tocopherols, tocotrienols, other chroman and side chain derivs. for use as antitumor agents and for inducing cell apoptosis)
RN 950-99-2 USPATFULL
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




=> **d his**

(FILE 'HOME' ENTERED AT 12:23:49 ON 27 AUG 2007)

FILE 'REGISTRY' ENTERED AT 12:24:10 ON 27 AUG 2007
L1 STRUCTURE UPLOADED
L2 8 S L1 EXA FULL

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 12:24:41 ON 27 AUG

2007
L3 511 S L2
L4 11 S L3 AND "PROSTATE CANCER"

=> **s l3 and "androgen-dependent"**
L5 1 L3 AND "ANDROGEN-DEPENDENT"

=> **d l5 ibib, abs, hitstr**

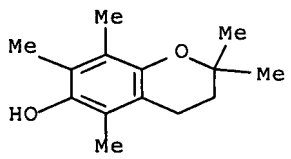
L5 ANSWER 1 OF 1 USPATFULL on STN
ACCESSION NUMBER: 2005:221605 USPATFULL Full-text
TITLE: Chroman-derived anti-androgens for treatment of androgen-mediated disorders
INVENTOR(S): Thompson, Todd A., Madison, WI, UNITED STATES
Wilding, George, Verona, WI, UNITED STATES
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation (U.S. corporation)

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2005192342 | A1 | 20050901 |
| APPLICATION INFO.: | US 2004-789835 | A1 | 20040227 (10) |

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 2003-450510P | 20030227 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: GODFREY & KAHN, S.C., 780 N. WATER STREET, MILWAUKEE, WI, 53202, US
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Page(s)
LINE COUNT: 1654
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods for the prevention and/or alleviation of androgen-mediated disorders treatable by administering a chroman-derived anti-androgen compound are provided by the present invention. The invention further provides pharmaceutical and nutraceutical compositions containing chroman-derived anti-androgen compounds useful in the prevention and/or alleviation of androgen-mediated disorders, particularly prostate cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 950-99-2, 2,2,5,7,8-Pentamethyl-6-chromanol
(chroman-derived antiandrogens for treatment of androgen-mediated disorders)
RN 950-99-2 USPATFULL
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)



=> **d his**

(FILE 'HOME' ENTERED AT 12:23:49 ON 27 AUG 2007)

FILE 'REGISTRY' ENTERED AT 12:24:10 ON 27 AUG 2007
L1 STRUCTURE UPLOADED
L2 8 S L1 EXA FULL

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 12:24:41 ON 27 AUG 2007
L3 511 S L2
L4 11 S L3 AND "PROSTATE CANCER"
L5 1 S L3 AND "ANDROGEN-DEPENDENT"

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| FULL ESTIMATED COST | 0.45 | 151.53 |

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STRUCTURE FILE UPDATES: 26 AUG 2007 HIGHEST RN 945604-45-5
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=> S 950-99-2/RN

L6 1 950-99-2/RN

=> SET NOTICE 1 DISPLAY

NOTICE SET TO 1 U.S. DOLLAR FOR DISPLAY COMMAND
SET COMMAND COMPLETED

=> D L6 SQIDE 1-

YOU HAVE REQUESTED DATA FROM 1 ANSWERS - CONTINUE? Y/(N):y
THE ESTIMATED COST FOR THIS REQUEST IS 6.55 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 950-99-2 REGISTRY
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 6-Chromanol, 2,2,5,7,8-pentamethyl- (6CI, 7CI, 8CI)
OTHER NAMES:
CN α-C-1-Chromanol
CN 2,2,5,7,8-Pentamethyl-6-chromanol
CN 2,2,5,7,8-Pentamethyl-6-hydroxychroman
CN 6-Hydroxy-2,2,5,7,8-pentamethylchroman
CN Chroman C1
CN Chromane C1
CN Chromanol
CN NSC 226236
CN PMC
CN TMC 5
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CI COM
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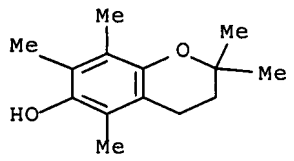
(*File contains numerically searchable property data)
DT.CA CAplus document type: Conference; Journal; Patent; Report
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

405 REFERENCES IN FILE CA (1907 TO DATE)
12 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
405 REFERENCES IN FILE CAPLUS (1907 TO DATE)
14 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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SET COMMAND COMPLETED

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=> **file medline caplus wpids uspatfull**

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| FULL ESTIMATED COST | 2.40 | 153.93 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
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FILE 'CAPLUS' ENTERED AT 12:44:38 ON 27 AUG 2007
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FILE 'USPATFULL' ENTERED AT 12:44:38 ON 27 AUG 2007
CA INDEXING COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

=> **s 16**
'RN' IS NOT A VALID FIELD CODE
L7  510 L6

=> **s 17 and (cancer or tumor)**
L8  22 L7 AND (CANCER OR TUMOR)

=> **d 18 1-22 ibib, abs, hitstr**

L8  ANSWER 1 OF 22  MEDLINE on STN
ACCESSION NUMBER:  2003400986  MEDLINE  Full-text
DOCUMENT NUMBER:  PubMed ID: 12939470
TITLE:  Androgen antagonist activity by the antioxidant moiety of vitamin E, 2,2,5,7,8-pentamethyl-6-chromanol in human prostate carcinoma cells.
AUTHOR:  Thompson Todd A; Wilding George
CORPORATE SOURCE:  University of Wisconsin Comprehensive Cancer Center, University of Wisconsin-Madison, Madison, Wisconsin 53792, USA.
SOURCE:  Molecular cancer therapeutics, (2003 Aug) Vol. 2, No. 8, pp. 797-803.
Journal code: 101132535. ISSN: 1535-7163.
PUB. COUNTRY:  United States
DOCUMENT TYPE:  Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE:  English
FILE SEGMENT:  Priority Journals
ENTRY MONTH:  200406
ENTRY DATE:  Entered STN: 27 Aug 2003
Last Updated on STN: 24 Jun 2004

Entered Medline: 21 Jun 2004

AB Antioxidants, such as vitamin E, are being investigated for efficacy in prostate cancer prevention. In this study, we show that the antioxidant moiety of vitamin E, 2,2,5,7,8-pentamethyl-6-chromanol (PMCol), has antiandrogen activity in prostate carcinoma cells. In the presence of PMCol, the androgen-stimulated biphasic growth curve of LNCaP human prostate carcinoma cells was shifted to the right. The PMCol-induced growth shift was similar to that produced by treatment with the pure antiandrogen bicalutamide (i.e., Casodex), indicative of androgen receptor (AR) antagonist activity. The concentration of PMCol used was below the concentration required to affect cell growth or viability in the absence of androgen. Using an AR binding competition assay, PMCol was found to be a potent antiandrogen in both LNCaP and LAPC4 cells, with an IC(50) of approximately 10 micro M against 1 nM R1881 (methyltrienolone; a stable, synthetic androgen). Prostate-specific antigen release from LNCaP cells produced by androgen exposure with either 0.05 or 1.0 nM R1881 was inhibited 100% and 80%, respectively, by 30 micro M PMCol. Also, PMCol inhibited androgen-induced promoter activation in both LNCaP and LAPC4 cells. However, PMCol did not affect AR protein levels, suggesting that the inhibitory effects of PMCol on androgenic pathways were not due to decreased expression of the AR. Therefore, growth modulation by the antioxidant moiety of vitamin E in androgen-sensitive prostate carcinoma cells is due, at least in part, to its potent antiandrogenic activity.

L8 ANSWER 2 OF 22 MEDLINE on STN

ACCESSION NUMBER: 95232770 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 7716769

TITLE: Phenoxyl radicals of etoposide (VP-16) can directly oxidize intracellular thiols: protective versus damaging effects of phenolic antioxidants.

AUTHOR: Tyurina Y Y; Tyurin V A; Yalowich J C; Quinn P J; Claycamp H G; Schor N F; Pitt B R; Kagan V E

CORPORATE SOURCE: Department of Environmental and Occupational Health, University of Pittsburgh, Pennsylvania 15238, USA.

SOURCE: Toxicology and applied pharmacology, (1995 Apr) Vol. 131, No. 2, pp. 277-88.
Journal code: 0416575. ISSN: 0041-008X.

PUB. COUNTRY: United States

DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199505

ENTRY DATE: Entered STN: 24 May 1995
Last Updated on STN: 3 Feb 1997
Entered Medline: 18 May 1995

AB Phenolic compounds can act as radical scavengers due to their ability to donate a mobile hydrogen to peroxyl radicals producing a phenoxyl radical if the phenoxyl radical formed in the radical scavenging reaction efficiently interacts with vitally important biomolecules, then this interaction may result in cytotoxic effects rather than in antioxidant protection. In the present work we have chosen two model compounds--a phenolic antitumor drug, VP-16, known to be highly cytotoxic, and a homolog of vitamin E, 2,2,5,7,8-pentamethyl-6-hydroxychromane (PMC)--as typical representatives of phenoxyl radicals to study interactions of their phenoxyl radicals with intracellular thiols. Using a water-soluble source of peroxyl radicals, the azo-initiator 2,2'-azobis(2- aminodinopropane) (AAPH), we found that both PMC and VP-16 are very efficient scavengers of peroxyl radicals as evidenced by their ability to inhibit AAPH-induced chemiluminescence of luminol and oxidation of PnA

incorporated into DOPC liposomes. Both PMC and VP-16 were also able to protect against AAPH-induced oxidative degradation of DNA in nuclei from human leukemic K562 cells. In contrast, there was a dramatic difference in the ability of VP-16 and PMC to protect GSH against AAPH-induced oxidation: while PMC inhibited AAPH-induced oxidation of GSH in a concentration-dependent manner, VP-16 did not protect GSH against oxidation. We hypothesized that this was due to different reactivities of the phenoxyl radicals formed by AAPH-derived peroxyl radicals from VP-16 and PMC toward GSH. To substantiate this hypothesis, we compared interactions of the phenoxyl radicals generated from VP-16 and PMC with intracellular thiols in K562 cell homogenates. While the PMC phenoxyl radicals were only slightly affected by thiols, the VP-16 phenoxyl radicals were reduced by thiols. This is evidenced by (i) a significant inhibition of the tyrosinase-induced VP-16 consumption upon addition of K562 cell homogenates, (ii) a depletion of endogenous thiols in K562 cell homogenates induced by VP-16+tyrosinase, (iii) a transient disappearance of the VP-16 phenoxyl radical signal from the ESR spectra and its reappearance after depletion of endogenous thiols, and (iv) elimination of the lag period for the appearance of the VP-16 phenoxyl radical ESR signal subsequent to depletion of thiols by mersalyl acid. To evaluate the contribution of GSH and protein thiols to reduction of the VP-GSH-peroxidase + cumeme hydroperoxide to specifically deplete endogenous GSH.(ABSTRACT TRUNCATED AT 400 WORDS)

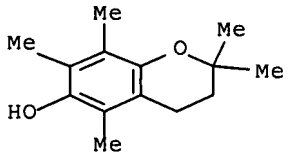
L8 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:101964 CAPLUS Full-text
DOCUMENT NUMBER: 144:184652
TITLE: Novel pathways in the etiology of cancer, and treatment methods
INVENTOR(S): Benz, Christopher C.
PATENT ASSIGNEE(S): Buck Institute for Age Research, USA
SOURCE: U.S. Pat. Appl. Publ., 49 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| US 2006024691 | A1 | 20060202 | US 2005-90546 | | 20050324 |
| PRIORITY APPLN. INFO.: | | | US 2004-556774P | P | 20040325 |
| | | | US 2004-580534P | P | 20040616 |
| | | | US 2004-629691P | P | 20041119 |

AB The invention pertains to the identification of two novel epithelial signaling pathways in ER-pos. breast cancers and the discovery that the cellular biol. and (likely also the clin. outcome) of ER-pos. breast cancer cells is unexpectedly altered when these signaling pathways are activated. The first pathway pertains to the discovery that NF-κB activation and/or DNA binding is implicated in the etiol. of ER-pos. breast (and other) cancers. The second pathway involves ligand-independent quinine-mediated ER activation by phosphorylation (e.g. on SER-118 and SER-167 residues of ER) and nuclear translocation of full-length (67 kDA) ER as well as the phorphorylating activation of a truncated and nuclear-localized ER variant (.apprx.52 kDa). Also disclosed are methods for identifying patients likely to respond to hormonal therapy and for selecting a therapeutic regimen for the treatment of cancer.

IT 950-99-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pathways in etiol. of cancer, and treatment methods)
RN 950-99-2 CAPLUS
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L8 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:120717 CAPLUS Full-text
DOCUMENT NUMBER: 142:170094
TITLE: Chroman-derived antiandrogens for treatment of androgen-mediated disorders
INVENTOR(S): Thompson, Todd A.; Wilding, George
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005011658 | A2 | 20050210 | WO 2004-US5872 | 20040227 |
| WO 2005011658 | A3 | 20050519 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
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| AU 2004260631 | A1 | 20050210 | AU 2004-260631 | 20040227 |
| CA 2517390 | A1 | 20050210 | CA 2004-2517390 | 20040227 |
| US 2005192342 | A1 | 20050901 | US 2004-789835 | 20040227 |
| EP 1596857 | A2 | 20051123 | EP 2004-785845 | 20040227 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |

PRIORITY APPLN. INFO.: US 2003-450510P P 20030227
WO 2004-US5872 A 20040227

OTHER SOURCE(S): MARPAT 142:170094

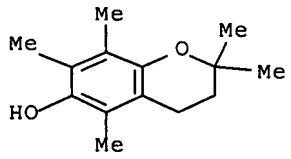
AB Methods for the prevention and/or alleviation of androgen-mediated disorders treatable by administering a chroman-derived antiandrogen compound are provided by the invention. The invention further provides pharmaceutical and nutraceutical compns. containing chroman-derived antiandrogen compds. useful in the prevention and/or alleviation of androgen-mediated disorders, particularly prostate cancer. Compds. of the invention include e.g. 2,2,5,7,8-pentamethyl-6-chromanol.

IT 950-99-2, 2,2,5,7,8-Pentamethyl-6-chromanol

RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chroman-derived antiandrogens for treatment of androgen-mediated disorders)

RN 950-99-2 CAPLUS

CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L8 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:618733 CAPLUS Full-text

DOCUMENT NUMBER: 141:174332

TITLE: Preparation of tocopherols, tocotrienols, other chroman and side chain derivatives for therapeutic use in the prevention and treatment of cancer

INVENTOR(S): Sanders, Bob G.; Kline, Kimberly; Hurley, Laurence; Gardner, Robb; Menchaca, Marla; Yu, Weiping; Ramanan, Puthucode N.; Liu, Shenquan; Israel, Karen

PATENT ASSIGNEE(S): Research Development Foundation, USA

SOURCE: U.S., 48 pp., Cont.-in-part of U.S. Ser. No. 404,001.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 6770672 | B1 | 20040803 | US 2000-502592 | 20000211 |
| US 6417223 | B1 | 20020709 | US 1999-404001 | 19990923 |
| CA 2399802 | A1 | 20010816 | CA 2001-2399802 | 20010209 |
| WO 2001058889 | A1 | 20010816 | WO 2001-US4168 | 20010209 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1254130 | A1 | 20021106 | EP 2001-909008 | 20010209 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004504268 | T | 20040212 | JP 2001-558439 | 20010209 |
| NZ 520798 | A | 20040528 | NZ 2001-520798 | 20010209 |
| CN 1529701 | A | 20040915 | CN 2001-807536 | 20010209 |
| RU 2263672 | C2 | 20051110 | RU 2002-124135 | 20010209 |
| US 2002107207 | A1 | 20020808 | US 2001-8066 | 20011105 |
| US 6703384 | B2 | 20040309 | | |

| | | | | |
|---|---|---|---|---|
| US 2004235938 | A1 | 20041125 | US 2003-644418 | 20030820 |
| US 2004097431 | A1 | 20040520 | US 2003-695275 | 20031028 |
| PRIORITY APPLN. INFO.: | | | US 1998-101543P | P 19980923 |
| | | | US 1999-404001 | A2 19990923 |
| | | | US 1998-101542P | P 19980923 |
| | | | US 2000-502592 | A 20000211 |
| | | | WO 2001-US4168 | W 20010209 |
| | | | US 2001-8066 | A3 20011105 |

OTHER SOURCE(S): MARPAT 141:174332

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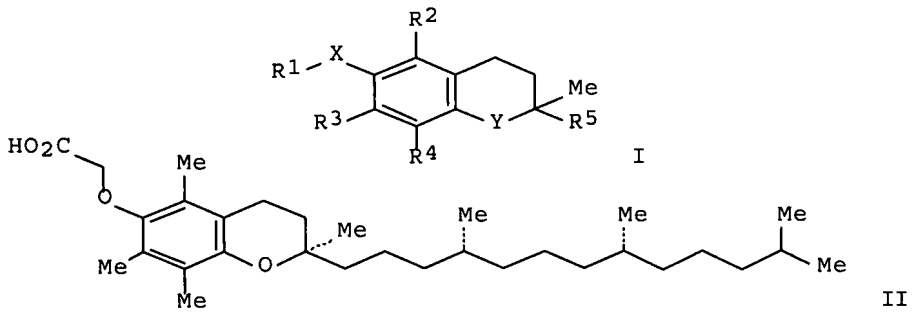
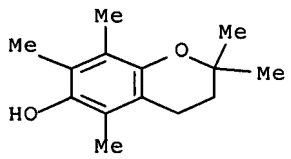



AB Chroman derivs., such as I [X = O, S, NR6; Y = O, NR6; R1 = carboxyalkyl, carboxyalkenyl, etc.; R2, R3, R4 = H, Me, alkyl, etc.; R5 = alkyl, alkenyl, etc.; R6 = H, alkyl], were prepared for use in antitumor pharmaceutical compns. for inducing apoptosis in a cell, particularly a cancer cell. Thus, α-tocopherol derivative II was prepared in 88% yield by a reaction of BrCH2CO2Me with (R,R,R)-α-tocopherol using NaOH in DMF. The prepared chromans were assayed for growth inhibitory and apoptotic activity against a variety of human cancer cell lines.

IT 950-99-2, 2,2,5,7,8-Pentamethyl-6-chromanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of tocopherols, tocotrienols, other chroman and side chain derivs. for therapeutic use in prevention and treatment of cancer)

RN 950-99-2 CAPLUS

CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:665773 CAPLUS Full-text

DOCUMENT NUMBER: 140:52950

TITLE: Androgen Antagonist Activity by the Antioxidant Moiety of Vitamin E, 2,2,5,7,8-Pentamethyl-6-chromanol in Human Prostate Carcinoma Cells

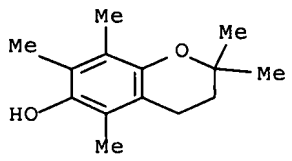
AUTHOR(S): Thompson, Todd A.; Wilding, George
CORPORATE SOURCE: University of Wisconsin Comprehensive Cancer Center and University of Wisconsin Department of Medicine, University of Wisconsin-Madison, Madison, WI, 53792, USA

SOURCE: Molecular Cancer Therapeutics (2003), 2(8), 797-803
CODEN: MCTOCF; ISSN: 1535-7163
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Antioxidants, such as vitamin E, are being investigated for efficacy in prostate cancer prevention. In this study, we show that the antioxidant moiety of vitamin E, 2,2,5,7,8-pentamethyl-6-chromanol (PMCol), has antiandrogen activity in prostate carcinoma cells. In the presence of PMCol, the androgen-stimulated biphasic growth curve of LNCaP human prostate carcinoma cells was shifted to the right. The PMCol-induced growth shift was similar to that produced by treatment with the pure antiandrogen bicalutamide (i.e., Casodex), indicative of androgen receptor (AR) antagonist activity. The concentration of PMCol used was below the concentration required to affect cell growth or viability in the absence of androgen. Using an AR binding competition assay, PMCol was found to be a potent antiandrogen in both LNCaP and LAPC4 cells, with an IC50 of approx. 10 μM against 1 nM R1881 (methyltrienolone; a stable, synthetic androgen). Prostate-specific antigen release from LNCaP cells produced by androgen exposure with either 0.05 or 1.0 nM R1881 was inhibited 100% and 80%, resp., by 30 μM PMCol. Also, PMCol inhibited androgen-induced promoter activation in both LNCaP and LAPC4 cells. However, PMCol did not affect AR protein levels, suggesting that the inhibitory effects of PMCol on androgenic pathways were not due to decreased expression of the AR. Therefore, growth modulation by the antioxidant moiety of vitamin E in androgen-sensitive prostate carcinoma cells is due, at least in part, to its potent antiandrogenic activity.

IT 950-99-2, 2,2,5,7,8-Pentamethyl-6-chromanol
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(androgen antagonist activity by the antioxidant moiety of vitamin E, 2,2,5,7,8-pentamethyl-6-chromanol in human prostate carcinoma cells)

RN 950-99-2 CAPLUS
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:595501 CAPLUS Full-text
DOCUMENT NUMBER: 137:140656
TITLE: Preparation of tocopherols, tocotrienols, other

chromans and side chain derivs. as potential antiproliferative and proapoptotic agents

INVENTOR(S): Sanders, Bob G.; Kline, Kimberly; Yu, Weiping

PATENT ASSIGNEE(S): Research Development Foundation, USA

SOURCE: U.S. Pat. Appl. Publ., 44 pp., Cont.-in-part of U. S. Ser. No. 502,592.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2002107207 | A1 | 20020808 | US 2001-8066 | 20011105 |
| US 6703384 | B2 | 20040309 | | |
| US 6417223 | B1 | 20020709 | US 1999-404001 | 19990923 |
| CN 1706838 | A | 20051214 | CN 2005-10003855 | 19990923 |
| US 6770672 | B1 | 20040803 | US 2000-502592 | 20000211 |
| US 2002156024 | A1 | 20021024 | US 2002-122019 | 20020412 |
| US 6645998 | B2 | 20031111 | | |
| WO 2003039461 | A2 | 20030515 | WO 2002-US35147 | 20021101 |
| WO 2003039461 | A3 | 20031113 | | |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002353971 | A1 | 20030519 | AU 2002-353971 | 20021101 |
| US 2004097431 | A1 | 20040520 | US 2003-695275 | 20031028 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1998-101542P | P | 19980923 |
| US 1999-404001 | A2 | 19990923 |
| US 2000-502592 | A2 | 20000211 |
| US 1998-101543P | P | 19980923 |
| CN 1999-812829 | A3 | 19990923 |
| US 2001-8066 | A | 20011105 |
| WO 2002-US35147 | W | 20021101 |

OTHER SOURCE(S): MARPAT 137:140656

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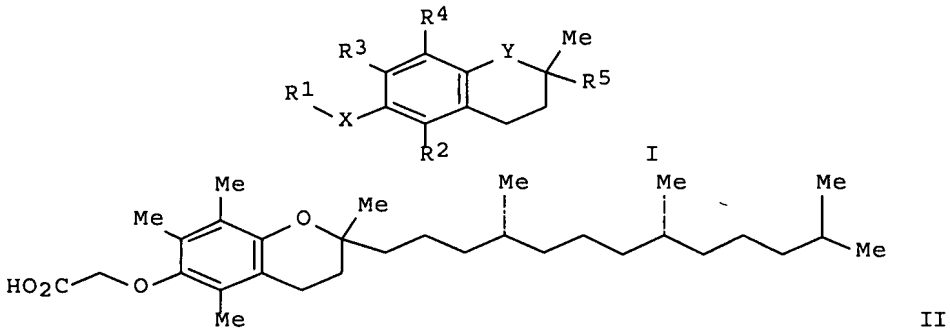
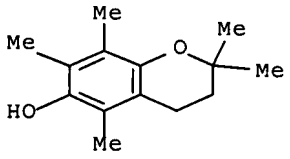


AB Derivs. of tocopherol, tocotrienol and other chromans of formula I (X and Y independently are oxygen, nitrogen or sulfur; when Y is nitrogen, nitrogen is substituted with R6 and R6 = H or Me; R1 = alkyl, alkenyl, alkynyl, aryl, heteroaryl, carboxylic acid, carboxylate, carboxamide, ester, thioamide, thiolacid, thiol ester, saccharide, alkoxy-linked saccharide, amine, sulfonate, sulfate, phosphate, alc., ethers or nitrites; R2, R3 = hydrogen or R4; R4 = Me, benzyl carboxylic acid, benzyl carboxylate, benzyl carboxamide, benzyl ester, saccharide or amine; and R5 = alkenyl) were prepared as antiproliferative and proapoptotic agents for the potential treatment of cell proliferative diseases. Thus, α-tocopherol was treated with Me bromoacetate and NaOH in N, N-dimethylformamide to give II. II showed effective growth inhibitory properties (apoptotic inducing) in a wide variety of human cancer cell lines, including breast, prostate, cervical, and ovarian cancers with EC50 values ranging from 1-20 μg/mL.

IT 950-99-2, 2,2,5,7,8-Pentamethyl-6-chromanol
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of tocopherols, tocotrienols, other chromans and side chain derivs. as potential antiproliferative, proapoptotic agents for the treatment of cancer)

RN 950-99-2 CAPLUS

CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L8 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:597976 CAPLUS Full-text

DOCUMENT NUMBER: 135:166941

TITLE: Preparation of tocopherols, tocotrienols, other chroman and side chain derivatives that induce cell apoptosis for therapeutic use as antiproliferative agents

INVENTOR(S): Sanders, Robert G.; Kline, Kimberly; Hurley, Laurence; Gardner, Robb; Menchaca, Marla; Yu, Weiping; Ramanan, Puthucode N.; Liu, Shenquan; Israel, Karen

PATENT ASSIGNEE(S): Research Development Foundation, USA

SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001058889 | A1 | 20010816 | WO 2001-US4168 | 20010209 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,

LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
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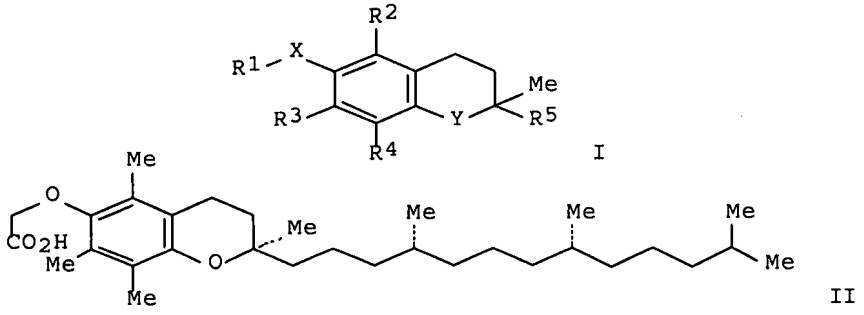
| US 6770672 | B1 | 20040803 | US 2000-502592 | | 20000211 |
| CA 2399802 | A1 | 20010816 | CA 2001-2399802 | | 20010209 |
| EP 1254130 | A1 | 20021106 | EP 2001-909008 | | 20010209 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | | |
| JP 2004504268 | T | 20040212 | JP 2001-558439 | | 20010209 |
| NZ 520798 | A | 20040528 | NZ 2001-520798 | | 20010209 |
| RU 2263672 | C2 | 20051110 | RU 2002-124135 | | 20010209 |
| PRIORITY APPLN. INFO.: | | | US 2000-502592 | A | 20000211 |
| | | | US 1998-101543P | P | 19980923 |
| | | | US 1999-404001 | A2 | 19990923 |
| | | | WO 2001-US4168 | W | 20010209 |

OTHER SOURCE(S): MARPAT 135:166941
GI



I

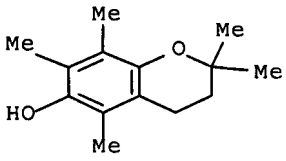
II

AB Tocopherol analogs, such as I [X = O, NH, S; Y = O, NH, S; R1 = alkyl, alkenyl, alkynyl, aryl, heteroaryl, carboxyl, carboxamide, thiocarboxyl, etc.; R2, R3, R4 = H, Me, benzyl, carboxyl, carboxamide, amine, saccharide; R5 = alkyl, alkenyl, alkynyl, aryl, heteroaryl, carboxyl, carboxamide], were prepared for pharmaceutical use as antiproliferative agents which induce cell apoptosis for treatment of cancers and diseases involving cell proliferation, such as autoimmune diseases, psoriasis, etc.. Thus, (R,R,R)-α-tocopherol derivative II was prepared in 88% yield by condensation of (R,R,R)-α-tocopherol and BrCH2CO2Me in DMF using NaOH followed by hydrolysis with 5 N HCl. The prepared tocopherol analogs were tested for their ability to induce apoptosis in a number of cancer cell lines, such as breast, cervical, colon, prostate, etc.

IT 950-99-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of tocopherols, tocotrienols, other chromans that induce cell apoptosis for therapeutic use as antiproliferative agents)

RN 950-99-2 CAPLUS

CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:209907 CAPLUS Full-text
DOCUMENT NUMBER: 132:237223
TITLE: Preparation of tocopherols, tocotrienols, other chroman and side chain derivatives for use as antitumor agents and for inducing cell apoptosis
INVENTOR(S): Kline, Kimberly; Sanders, Bob G.; Hurley, Laurence; Gardner, Robb; Menchaca, Marla; Yu, Weiping; Ramanan, Puthucode N.; Liu, Shenquan; Israel, Karen
PATENT ASSIGNEE(S): Research Development Foundation, USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000016772 | A1 | 20000330 | WO 1999-US21778 | 19990923 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW | | | | |
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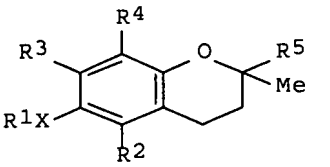
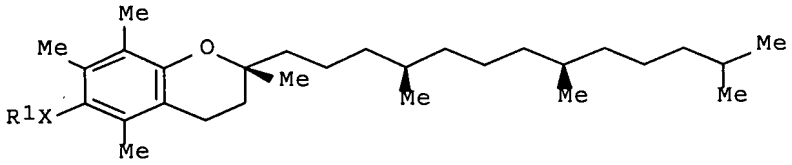
| CA 2345079 | A1 | 20000330 | CA 1999-2345079 | 19990923 |
| AU 9961553 | A1 | 20000410 | AU 1999-61553 | 19990923 |
| AU 757013 | B2 | 20030130 | | |
| EP 1115398 | A1 | 20010718 | EP 1999-948352 | 19990923 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| CN 1325303 | A | 20011205 | CN 1999-812829 | 19990923 |
| JP 2002526446 | T | 20020820 | JP 2000-573733 | 19990923 |
| NZ 510732 | A | 20040130 | NZ 1999-510732 | 19990923 |
| RU 2232758 | C2 | 20040720 | RU 2001-111019 | 19990923 |
| CN 1706838 | A | 20051214 | CN 2005-10003855 | 19990923 |
| IL 142082 | A | 20051218 | IL 1999-142082 | 19990923 |
| TW 592695 | B | 20040621 | TW 1999-88120073 | 19991117 |
| ZA 2001002057 | A | 20020319 | ZA 2001-2057 | 20010313 |
| PRIORITY APPLN. INFO.: | | | US 1998-101542P P | 19980923 |
| | | | CN 1999-812829 A3 | 19990923 |
| | | | WO 1999-US21778 W | 19990923 |

OTHER SOURCE(S): MARPAT 132:237223
GI



I



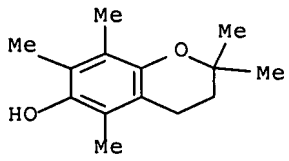
II

AB Chromans I [R1 = alkyl, alkenyl, alkynyl, aryl, herteroaryl, carboxyl, carboxamide, thioamide, saccharide, amine, sulfate, phosphate, etc.; R2, R3, R4 = H, Me, benzylcarboxylate, saccharide, amino, etc.; R5 = alkyl, alkenyl, alkynyl, aryl, herteroaryl, carboxyl, carboxamide; X = O, NH, S] were prepared for pharmaceutical use as antitumor agents and cell apoptosis inducing agents. Thus, tocopherol derivative II (R1 = CH2CO2H, X = O) was prepared in 88% yield via O-alkylation of (+)-α-tocopherol with Me bromoacetate. The prepared chromans were tested for cell apoptosis activity against a variety of cancer cell lines.

IT 950-99-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of tocopherols, tocotrienols, other chroman and side chain derivs. for use as antitumor agents and for inducing cell apoptosis)

RN 950-99-2 CAPLUS

CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:602318 CAPLUS Full-text

DOCUMENT NUMBER: 131:295249

TITLE: Mechanism-based chemopreventive strategies against etoposide-induced acute myeloid leukemia: free radical/antioxidant approach

AUTHOR(S): Kagan, Valerian E.; Yalowich, Jack C.; Borisenko, Grigory G.; Tyurina, Yulia Y.; Tyurin, Vladimir A.; Thampatty, Padmakumari; Fabisiak, James P.

CORPORATE SOURCE: Departments of Environmental and Occupational Health and Pharmacology and University of Pittsburgh Cancer Institute, University of Pittsburgh, Pittsburgh, PA, USA

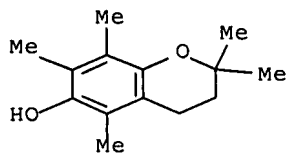
SOURCE: Molecular Pharmacology (1999), 56(3), 494-506
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Etoposide (VP-16) is extensively used to treat cancer, yet its efficacy is calamitously associated with an increased risk of secondary acute myelogenous leukemia. The mechanisms for the extremely high susceptibility of myeloid stem cells to the leukemogenic effects of etoposide have not been elucidated. We propose a mechanism to account for the etoposide-induced secondary acute myelogenous leukemia and nutritional strategies to prevent this complication of etoposide therapy. We hypothesize that etoposide phenoxyl radicals (etoposide-O) formed from etoposide by myeloperoxidase are responsible for its genotoxic effects in bone marrow progenitor cells, which contain constitutively high myeloperoxidase activity. Here, we used purified human myeloperoxidase, as well as human leukemia HL60 cells with high myeloperoxidase activity and provide evidence of the following. 1. Etoposide undergoes one-electron oxidation to etoposide-O· catalyzed by both purified myeloperoxidase and myeloperoxidase activity in HL60 cells; formation of etoposide-O·radicals is completely blocked by myeloperoxidase inhibitors, cyanide and azide. 2. Intracellular reductants, GSH and protein sulfhydryls (but not phospholipids), are involved in myeloperoxidase-catalyzed etoposide redox-cycling that oxidizes endogenous thiols; pretreatment of HL60 cells with a maleimide thiol reagent, ThioGlo1, prevents redox-cycling of etoposide-O· radicals and permits their direct ESR detection in cell homogenates. VP-16 redox-cycling by purified myeloperoxidase (in the presence of GSH) or by myeloperoxidase activity in HL60 cells is accompanied by generation of thiyl radicals, GS·, determined by HPLC assay of 5,5-dimethyl-1- pyrroline glytathionyl N-oxide glytathionyl nitrone adducts. 3. Ascorbate directly reduces etoposide-O·, thus competitively inhibiting etoposide-O·-induced thiol oxidation Ascorbate also diminishes etoposide-induced topo II-DNA complex formation in myeloperoxidase-rich HL60 cells (but not in HL60 cells with myeloperoxidase activity depleted by pretreatment with succinyl acetone). 4. A vitamin E homolog, 2,2,5,7,8-pentamethyl-6-hydroxychromane, a hindered phenolic compound whose phenoxyl radicals do not oxidize endogenous thiols, effectively competes with etoposide as a substrate for myeloperoxidase, thus preventing etoposide-O·-induced redox-cycling. We conclude that nutritional antioxidant strategies can be targeted at minimizing etoposide conversion to etoposide-O·, thus minimizing the genotoxic effects of the radicals in bone marrow myelogenous progenitor cells, i.e., chemoprevention of etoposide-induced acute myelogenous leukemia.

IT 950-99-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanism-based chemopreventive strategies against etoposide-induced acute myeloid leukemia: free radical/antioxidant approach)

RN 950-99-2 CAPLUS

CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)

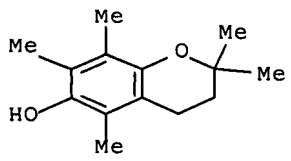


REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:440374 CAPLUS Full-text
DOCUMENT NUMBER: 119:40374
TITLE: Inhibition of NF-κB activation by vitamin E derivatives
AUTHOR(S): Suzuki, Yuichiro J.; Packer, Lester
CORPORATE SOURCE: Dep. Mol. Cell Biol., Univ. California, Berkeley, CA, 94720, USA
SOURCE: Biochemical and Biophysical Research Communications (1993), 193(1), 277-83
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Nuclear factor κB (NF-κB) is believed to play an important role in the activation of a human immunodeficiency virus (HIV) which causes acquired immunodeficiency syndrome (AIDS). Recent findings suggesting an involvement of reactive oxygen species in signal transduction pathways leading to NF-κB activation have ensured the possible clin. use of antioxidants in blocking HIV activation. The present study examined the effects of vitamin E derivs. on the tumor necrosis factor-α (TNF-α)-induced NF-κB activation. Incubation of human Jurkat T cells with vitamin E acetate or α-tocopheryl succinate (10 μM to 1 mM) exhibited a concentration-dependent inhibition of NK-κB activation. α-Tocopherol or succinate at these concns. had no apparent effects. 2,2,5,7,8-Pentamethyl-6-hydroxychromane (PMC) was extremely effective, causing complete inhibition of NK-κB activation at 10 μM. Oct-1 binding activity was inactivated by α-tocopheryl succinate whereas other derivs. had no effects, suggesting that the effects of α-tocopheryl succinate are not specific to NF-κB. HPLC measurements demonstrated that treatment of cells with TNF-α had no effects on cellular α-tocopherol, but vitamin E acetate treatment increased the α-tocopherol content. Cell viability was not affected by any of the vitamin E derivs. These results indicate a possible use of vitamin E derivs. in AIDS therapeutics.

IT 950-99-2
RL: BIOL (Biological study)
(TNF-α-induced nuclear factor κB activation inhibition by, AIDS therapy in relation to)
RN 950-99-2 CAPLUS
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L8 ANSWER 12 OF 22 USPATFULL on STN
ACCESSION NUMBER: 2006:289167 USPATFULL Full-text
TITLE: Use of active ingredients for the prophylaxis and/or

therapy of viral diseases

INVENTOR(S): Planz, Oliver, Wendelsheimer Strasse 34, Rottenburg, GERMANY, FEDERAL REPUBLIC OF 72108
Pleschka, Stephan, Giessen, GERMANY, FEDERAL REPUBLIC OF
Sedlacek, Hans-Harald, Marburg, GERMANY, FEDERAL REPUBLIC OF
Ludwig, Stephan, Wurzeburg, GERMANY, FEDERAL REPUBLIC OF
PATENT ASSIGNEE(S): Inamed GmbH Institut Fur Aerosolmedizin, Gemunden, GERMANY, FEDERAL REPUBLIC OF, D-35285 (non-U.S. corporation)

| | NUMBER | KIND | DATE | |
|---|---|---|---|---|
| PATENT INFORMATION: | US 2006247161 | A1 | 20061102 | |
| APPLICATION INFO.: | US 2004-541633 | A1 | 20040102 | (10) |
| | WO 2004-DE12 | | 20040102 | |
| | | | 20060630 | PCT 371 date |

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | DE 2003-10300222 | 20030103 |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MAYER & WILLIAMS PC, 251 NORTH AVENUE WEST, 2ND FLOOR, WESTFIELD, NJ, 07090, US
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
LINE COUNT: 781

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

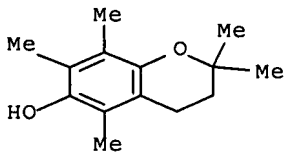
AB The invention relates to the use preferably of at least one active ingredient for the prophylaxis and/or therapy of a viral disease, wherein this active ingredient inhibits at least one component of the cellular signal transduction pathway for the activation of the transcription factor NF-kB such that the virus multiplication is inhibited. The present invention relates furthermore to the local, preferably aerogenic administration of the active ingredient according to the invention for inhibiting a virus multiplication. The active ingredient according to the invention may be combined with at least one further antivirally effective substance for the prophylaxis and/or therapy of a viral disease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 950-99-2
(inhibitor of component of signal transduction for activation of NF-kB for prophylaxisnd/or therapy of virus diseases)

RN 950-99-2 USPATFULL

CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)



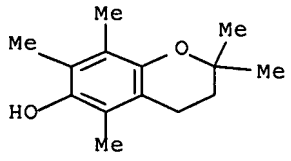
L8 ANSWER 13 OF 22 USPATFULL on STN
ACCESSION NUMBER: 2006:227433 USPATFULL Full-text
TITLE: Chroman derivatives as lipoxygenase inhibitors
INVENTOR(S): Zhang, Wei, Santa Clara, CA, UNITED STATES
Chen, Jian, San Jose, CA, UNITED STATES
Boddupalli, Sekhar, San Jose, CA, UNITED STATES
PATENT ASSIGNEE(S): Galileo Pharmaceuticals, Inc (U.S. corporation)

| | NUMBER | KIND | DATE | |
|---|---|---|---|---|
| PATENT INFORMATION: | US 2006193797 | A1 | 20060831 | |
| APPLICATION INFO.: | US 2006-349813 | A1 | 20060207 | (11) |

| | NUMBER | DATE | |
|---|---|---|---|
| PRIORITY INFORMATION: | US 2005-656644P | 20050225 | (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FOLEY & LARDNER LLP, 1530 PAGE MILL ROAD, PALO ALTO, CA, 94304, US
NUMBER OF CLAIMS: 48
EXEMPLARY CLAIM: 1
LINE COUNT: 2649
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is concerned with certain novel derivatives of Formula I: ##STR1## wherein X and R.sup.1 to R.sup.10 are as described in the specification, and where either R.sup.5 is OH, --NR.sup.dOR.sup.a or --NR.sup.d--NR.sup.bR.sup.c, or R.sup.7 is --NR.sup.dOR.sup.a or --NR.sup.d--NR.sup.bR.sup.c, or C.dbd.R.sup.7R.sup.8 is C.dbd.NOR.sup.a or C.dbd.N--NR.sup.bR.sup.c, which may be useful in the manufacture of pharmaceutical compositions for treating disorders mediated by lipoxygenases. They may also be useful in the manufacture of skin care and/or pharmaceutical compositions for the treatment of lipoxygenase mediated disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 950-99-2, 2,2,5,7,8-Pentamethylchroman-6-ol
(skin care and pharmaceutical compns. comprising chroman derivs. as lipoxygenase inhibitors)
RN 950-99-2 USPATFULL
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L8 ANSWER 14 OF 22 USPATFULL on STN
ACCESSION NUMBER: 2006:27860 USPATFULL Full-text
TITLE: Novel pathways in the etiology of cancer
INVENTOR(S): Benz, Christopher C., Novato, CA, UNITED STATES
PATENT ASSIGNEE(S): Buck Institute for Age Research (U.S. corporation)

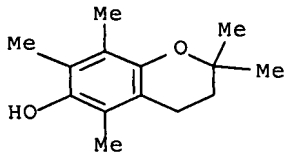
| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2006024691 | A1 | 20060202 |
| APPLICATION INFO.: | US 2005-90546 | A1 | 20050324 (11) |

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 2004-556774P | 20040325 (60) |
| | US 2004-580534P | 20040616 (60) |
| | US 2004-629691P | 20041119 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C., P O BOX 458, ALAMEDA, CA, 94501, US
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 19 Drawing Page(s)
LINE COUNT: 2824
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention pertains to the identification of two novel epithelial signaling pathways in ER-positive breast cancer s and the discovery that the cellular biology and (likely also the clinical outcome) of ER-positive breast cancer cells is unexpectedly altered when these signaling pathways are activated. The first pathway pertains to the discovery that NF-κB activation and/or DNA binding is implicated in the etiology of ER-positive breast (and other) cancers. The second pathway involves ligand-independent quinine-mediated ER activation by posphorylation (e.g. on SER-118 and SER-167 residues of ER) and nuclear translocation of full-length (67 kDA) ER as well as the phorphorylating activation of a truncated and nuclear-localized ER variant (.about.52 kDa).

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 950-99-2
(pathways in etiol. of cancer, and treatment methods)
RN 950-99-2 USPATFULL
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L8 ANSWER 15 OF 22 USPATFULL on STN
ACCESSION NUMBER: 2005:221605 USPATFULL Full-text
TITLE: Chroman-derived anti-androgens for treatment of androgen-mediated disorders
INVENTOR(S): Thompson, Todd A., Madison, WI, UNITED STATES
Wilding, George, Verona, WI, UNITED STATES
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation (U.S. corporation)

| | NUMBER | KIND | DATE |
|---|---|---|---|

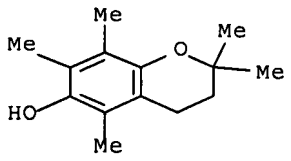
PATENT INFORMATION: US 2005192342 A1 20050901
APPLICATION INFO.: US 2004-789835 A1 20040227 (10)

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 2003-450510P | 20030227 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: GODFREY & KAHN, S.C., 780 N. WATER STREET, MILWAUKEE, WI, 53202, US
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 8 Drawing Page(s)
LINE COUNT: 1654
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods for the prevention and/or alleviation of androgen-mediated disorders treatable by administering a chroman-derived anti-androgen compound are provided by the present invention. The invention further provides pharmaceutical and nutraceutical compositions containing chroman-derived anti-androgen compounds useful in the prevention and/or alleviation of androgen-mediated disorders, particularly prostate cancer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 950-99-2, 2,2,5,7,8-Pentamethyl-6-chromanol
(chroman-derived antiandrogens for treatment of androgen-mediated disorders)
RN 950-99-2 USPATFULL
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L8 ANSWER 16 OF 22 USPATFULL on STN
ACCESSION NUMBER: 2004:300069 USPATFULL Full-text
TITLE: Tocopherols, tocotrienols, other chroman and side chain derivatives and uses thereof
INVENTOR(S): Sanders, Bob G., Austin, TX, UNITED STATES
Kline, Kimberly, Austin, TX, UNITED STATES
Hurley, Laurence, Austin, TX, UNITED STATES
Gardner, Robb, Austin, TX, UNITED STATES
Menchaca, Marla, Austin, TX, UNITED STATES
Yu, Weiping, Austin, TX, UNITED STATES
Ramanan, Puthucode N., Austin, TX, UNITED STATES
Liu, Shenquan, Austin, TX, UNITED STATES
Israel, Karen, Austin, TX, UNITED STATES
PATENT ASSIGNEE(S): Research Development Foundation (U.S. corporation)

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2004235938 | A1 | 20041125 |
| APPLICATION INFO.: | US 2003-644418 | A1 | 20030820 (10) |

RELATED APPLN. INFO.: Division of Ser. No. US 2000-502592, filed on 11 Feb 2000, GRANTED, Pat. No. US 6770672 Continuation-in-part of Ser. No. US 1999-404001, filed on 23 Sep 1999, GRANTED, Pat. No. US 6417223

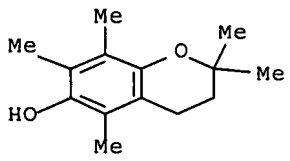
| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1998-101542P | 19980923 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Benjamin Aaron Adler, ADLER & ASSOCIATES, 8011 Candle Lane, Houston, TX, 77071
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 21 Drawing Page(s)
LINE COUNT: 2556
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides an antiproliferative compound having the structural formula ##STR1##

wherein X is oxygen, nitrogen or sulfur; Y is selected from the group consisting of oxygen, nitrogen and sulfur wherein when Y is oxygen or nitrogen, n is 1 and when Y is sulfur, n is 0. Also provided is a method for inducing apoptosis in a cell comprising administering a composition comprising a compound.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 950-99-2
(preparation of tocopherols, tocotrienols, other chroman and side chain derivs. for use as antitumor agents and for inducing cell apoptosis)
RN 950-99-2 USPATFULL
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L8 ANSWER 17 OF 22 USPATFULL on STN
ACCESSION NUMBER: 2004:192666 USPATFULL Full-text
TITLE: Tocopherols, tocotrienols, other chroman and side chain derivatives and uses thereof
INVENTOR(S): Sanders, Bob G., Austin, TX, United States
Kline, Kimberly, Austin, TX, United States
Hurley, Laurence, Austin, TX, United States
Gardner, Robb, Austin, TX, United States
Menchaca, Marla, Austin, TX, United States
Yu, Weiping, Austin, TX, United States
Ramanan, Puthucode N., Austin, TX, United States
Liu, Shenquan, Austin, TX, United States
Israel, Karen, Austin, TX, United States
PATENT ASSIGNEE(S): Research Development Foundation, Carson City, NV,

United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 6770672 | B1 | 20040803 |
| APPLICATION INFO.: | US 2000-502592 | | 20000211 (9) |

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1999-404001, filed on 23 Sep 1999, now patented, Pat. No. US 6417223, issued on 9 Jul 2002

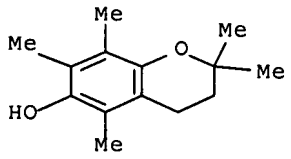
| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1998-101543P | 19980923 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Fonda, Kathleen K.
ASSISTANT EXAMINER: Maier, Leigh C.
LEGAL REPRESENTATIVE: Adler, Benjamin Aaron
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 18 Drawing Figure(s); 21 Drawing Page(s)
LINE COUNT: 2359
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides an antiproliferative compound having the structural formula ##STR1##

wherein X is oxygen, nitrogen or sulfur; Y is selected from the group consisting of oxygen, nitrogen and sulfur wherein when Y is oxygen or nitrogen, n is 1 and when Y is sulfur, n is 0. Also provided is a method for inducing apoptosis in a cell comprising administering a composition comprising a compound.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 950-99-2, 2,2,5,7,8-Pentamethyl-6-chromanol
(preparation of tocopherols, tocotrienols, other chroman and side chain derivs. for therapeutic use in prevention and treatment of cancer)
RN 950-99-2 USPATFULL
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L8 ANSWER 18 OF 22 USPATFULL on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2004:127448 USPATFULL Full-text |
| TITLE: | Tocopherols, tocotrienols, other chroman and side chain derivatives and uses thereof |
| INVENTOR(S): | Sanders, Bob G., Austin, TX, UNITED STATES<br>Kline, Kimberly, Austin, TX, UNITED STATES<br>Yu, Weiping, Austin, TX, UNITED STATES |
| PATENT ASSIGNEE(S): | Research Development Foundation (U.S. corporation) |

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2004097431 | A1 | 20040520 |
| APPLICATION INFO.: | US 2003-695275 | A1 | 20031028 (10) |

RELATED APPLN. INFO.: Division of Ser. No. US 2001-8066, filed on 5 Nov 2001, GRANTED, Pat. No. US 6703384 Continuation-in-part of Ser. No. US 2000-502592, filed on 11 Feb 2000, PENDING Continuation-in-part of Ser. No. US 1999-404001, filed on 23 Sep 1999, GRANTED, Pat. No. US 6417223

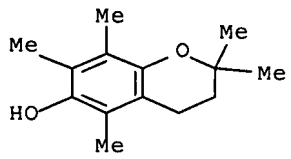
| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1998-101542P | 19980923 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Benjamin Aaron Adler, Ph.D., J.D., Adler & Associates, 8011 Candle Lane, Houston, TX, 77071
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Page(s)
LINE COUNT: 2605
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides an antiproliferative compound having a structural formula ##STR1##

where X and Y independently are oxygen, nitrogen or sulfur; R.sup.1 is alkyl, alkenyl, alkynyl, aryl, heteroaryl, carboxylic acid, carboxylate, carboxamide, ester, thioamide, thiolacid, thiolester, saccharide, alkoxy-linked saccharide, amine, sulfonate, sulfate, phosphate, alcohol, ethers or nitrites; R.sup.2 and R.sup.3 are hydrogen or R.sup.4; R.sup.4 is methyl, benzyl carboxylic acid, benzyl carboxylate, benzyl carboxamide, benzylester, saccharide or amine; and R.sup.5 is alkenyl; where when Y is nitrogen, said nitrogen is substituted with R.sup.6, wherein R.sup.6 is hydrogen or methyl. Also provided are methods for treating a cell proliferative disease and for inducing apoptosis in a cell comprising administering this compound is also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 950-99-2
(preparation of tocopherols, tocotrienols, other chroman and side chain derivs. for use as antitumor agents and for inducing cell apoptosis)
RN 950-99-2 USPATFULL
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L8 ANSWER 19 OF 22 USPATFULL on STN
ACCESSION NUMBER: 2002:280579 USPATFULL Full-text

TITLE: Tocopherols, tocotrienols, other chroman and side chain derivatives and uses thereof

INVENTOR(S): Sanders, Bob G., Austin, TX, UNITED STATES
Kline, Kimberly, Austin, TX, UNITED STATES
Hurley, Laurence, Austin, TX, UNITED STATES
Gardner, Robb, Austin, TX, UNITED STATES
Menchaca, Marla, Austin, TX, UNITED STATES
Yu, Weiping, Austin, TX, UNITED STATES
Ramanan, Puthucode N., Austin, TX, UNITED STATES
Liu, Shenquan, Austin, TX, UNITED STATES
Israel, Karen, Austin, TX, UNITED STATES
PATENT ASSIGNEE(S): Research Development Foundation (U.S. corporation)

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2002156024 | A1 | 20021024 |
| | US 6645998 | B2 | 20031111 |
| APPLICATION INFO.: | US 2002-122019 | A1 | 20020412 (10) |

RELATED APPLN. INFO.: Division of Ser. No. US 1999-404001, filed on 23 Sep 1999, GRANTED, Pat. No. US 6417223

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1998-101542P | 19980923 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Benjamin Aaron Adler, ADLER & ASSOCIATES, 8011 Candle Lane, Houston, TX, 77071
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 14 Drawing Page(s)
LINE COUNT: 2170

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

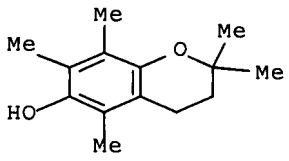
AB The present invention provides an antiproliferative compound having the structural formula ##STR1##

wherein X is oxygen, nitrogen or sulfur; R.sup.1 is alkyl, alkenyl, alkynyl, aryl, heteroaryl, carboxylic acid, carboxylate, carboxamide, ester, thioamide, thiolacid, thiolester, saccharide, alkoxy-linked saccharide, amine, sulfonate, sulfate, phosphate, alcohol, ethers and nitriles; R.sup.2 is hydrogen, methyl, benzyl carboxylic acid, benzyl carboxylate, benzyl carboxamide, benzylester, saccharide and amine; R.sup.3 is selected from the group consisting of hydrogen, methyl, benzyl carboxylic acid, benzyl carboxylate, benzyl carboxamide, benzylester, saccharide and amine; R.sup.4 is of methyl, benzyl carboxylic acid, benzyl carboxylate, benzyl carboxamide, benzylester, saccharide and amine; and R.sup.5 is alkyl, alkenyl, alkynyl, aryl, heteroaryl, carboxyl, amide and ester. Also provided is a method for inducing apoptosis in a cell comprising administering a composition comprising a compound.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 950-99-2
(preparation of tocopherols, tocotrienols, other chroman and side chain derivs. for use as antitumor agents and for inducing cell apoptosis)

RN 950-99-2 USPATFULL
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L8 ANSWER 20 OF 22 USPATFULL on STN

| | |
|---|---|
| ACCESSION NUMBER: | 2002:199098 USPATFULL Full-text |
| TITLE: | Tocopherols, tocotrienols, other chroman and side chain derivatives and uses thereof |
| INVENTOR(S): | Sanders, Bob G., Austin, TX, UNITED STATES<br>Kline, Kimberly, Austin, TX, UNITED STATES<br>Yu, Weiping, Austin, TX, UNITED STATES |

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2002107207 | A1 | 20020808 |
| | US 6703384 | B2 | 20040309 |
| APPLICATION INFO.: | US 2001-8066 | A1 | 20011105 (10) |

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2000-502592, filed on 11 Feb 2000, PENDING Continuation-in-part of Ser. No. US 1999-404001, filed on 23 Sep 1999, PENDING

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1998-101542P | 19980923 (60) |

| | |
|---|---|
| DOCUMENT TYPE: | Utility |
| FILE SEGMENT: | APPLICATION |
| LEGAL REPRESENTATIVE: | Benjamin Aaron Adler, ADLER & ASSOCIATES, 8011 Candle Lane, Houston, TX, 77071 |
| NUMBER OF CLAIMS: | 24 |
| EXEMPLARY CLAIM: | 1 |
| NUMBER OF DRAWINGS: | 12 Drawing Page(s) |
| LINE COUNT: | 2606 |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

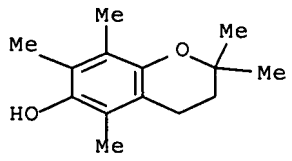
AB The present invention provides an antiproliferative compound having a structural formula ##STR1##

where X and Y independently are oxygen, nitrogen or sulfur; R.sup.1 is alkyl, alkenyl, alkynyl, aryl, heteroaryl, carboxylic acid, carboxylate, carboxamide, ester, thioamide, thiolacid, thiolester, saccharide, alkoxy-linked saccharide, amine, sulfonate, sulfate, phosphate, alcohol, ethers or nitrites; R.sup.2 and R.sup.3 are hydrogen or R.sup.4; R.sup.4 is methyl, benzyl carboxylic acid, benzyl carboxylate, benzyl carboxamide, benzylester, saccharide or amine; and R.sup.5 is alkenyl; where when Y is nitrogen, said nitrogen is substituted with R.sup.6, wherein R.sup.6 is hydrogen or methyl. Also provided are methods for treating a cell proliferative disease and for inducing apoptosis in a cell comprising administering this compound is also provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 950-99-2, 2,2,5,7,8-Pentamethyl-6-chromanol
(preparation of tocopherols, tocotrienols, other chromans and side chain derivs. as potential antiproliferative, proapoptotic agents for the

treatment of cancer)
RN 950-99-2 USPATFULL
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L8 ANSWER 21 OF 22 USPATFULL on STN
ACCESSION NUMBER: 2002:168253 USPATFULL Full-text
TITLE: Tocopherols, tocotrienols, other chroman and side chain derivatives and uses therof
INVENTOR(S): Sanders, Bob G., Austin, TX, United States
Kline, Kimberly, Austin, TX, United States
Hurley, Laurence, Austin, TX, United States
Gardner, Robb, Austin, TX, United States
Menchaca, Marla, Austin, TX, United States
Yu, Weiping, Austin, TX, United States
Ramanan, Puthucode N., Austin, TX, United States
Liu, Shenquan, Austin, TX, United States
Israel, Karen, Austin, TX, United States
PATENT ASSIGNEE(S): Research Development Foundation, Carson City, NV, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 6417223 | B1 | 20020709 |
| APPLICATION INFO.: | US 1999-404001 | | 19990923 (9) |

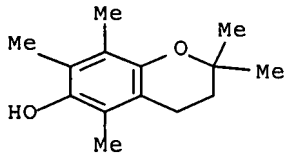
| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1998-101542P | 19980923 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Wilson, James O.
ASSISTANT EXAMINER: Maier, Leigh C.
LEGAL REPRESENTATIVE: Adler, Benjamin Aaron
NUMBER OF CLAIMS: 3
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 14 Drawing Figure(s); 14 Drawing Page(s)
LINE COUNT: 1959
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides an antiproliferative compound having the structural formula ##STR1##

wherein X is oxygen, nitrogen or sulfur; R.sup.1 is alkyl, alkenyl, alkynyl, aryl, heteroaryl, carboxylic acid, carboxylate, carboxamide, ester, thioamide, thiolacid, thiolester, saccharide, alkoxy-linked saccharide, amine, sulfonate, sulfate, phosphate, alcohol, ethers and nitriles; R.sup.2 is hydrogen, methyl, benzyl carboxylic acid, benzyl carboxylate, benzyl carboxamide, benzylester, saccharide and amine; R.sup.3 is selected from the group consisting of hydrogen, methyl, benzyl carboxylic acid, benzyl

carboxylate, benzyl carboxamide, benzylester, saccharide and amine; R.sup.4 is of methyl, benzyl carboxylic acid, benzyl carboxylate, benzyl carboxamide, benzylester, saccharide and amine; and R.sup.5 is alkyl, alkenyl, alkynyl, aryl, heteroaryl, carboxyl, amide and ester. Also provided is a method for inducing apoptosis in a cell comprising administering a composition comprising a compound.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 950-99-2
(preparation of tocopherols, tocotrienols, other chroman and side chain derivs. for use as antitumor agents and for inducing cell apoptosis)
RN 950-99-2 USPATFULL
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




L8 ANSWER 22 OF 22 USPATFULL on STN
ACCESSION NUMBER: 92:55640 USPATFULL Full-text
TITLE: Oxidized diphenylheteroalkanes
INVENTOR(S): Janssen, Bernd, Ludwigshafen, Germany, Federal Republic of
Wuest, Hans-Heiner, Dossenheim, Germany, Federal Republic of
PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Ludwigshafen, Germany, Federal Republic of (non-U.S. corporation)

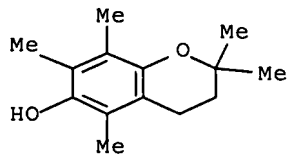
| | NUMBER | KIND | DATE | |
|---|---|---|---|---|
| PATENT INFORMATION: | US 5128479 | | 19920707 | |
| APPLICATION INFO.: | US 1990-471886 | | 19900129 | (7) |

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | DE 1989-3903988 | 19890210 |

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Raymond, Richard L.
LEGAL REPRESENTATIVE: Oblon, Spivak, McClelland, Maier & Neustadt
NUMBER OF CLAIMS: 4
EXEMPLARY CLAIM: 1
LINE COUNT: 1176
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Oxidized diphenylheteroalkanes of the formula I ##STR1## where R.sup.1 to R.sup.6 and A have the meanings specified in the description, and the preparation thereof are described. The substances are suitable for controlling diseases and as cosmetic agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT 950-99-2P, 2,2,5,7,8-Pentamethylchroman-6-ol

(preparation and reaction of, in preparation of drugs)
RN 950-99-2 USPATFULL
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,2,5,7,8-pentamethyl- (CA INDEX NAME)




=> **d his**

(FILE 'HOME' ENTERED AT 12:23:49 ON 27 AUG 2007)

FILE 'REGISTRY' ENTERED AT 12:24:10 ON 27 AUG 2007
L1 STRUCTURE UPLOADED
L2 8 S L1 EXA FULL

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 12:24:41 ON 27 AUG 2007
L3 511 S L2
L4 11 S L3 AND "PROSTATE CANCER"
L5 1 S L3 AND "ANDROGEN-DEPENDENT"

FILE 'REGISTRY' ENTERED AT 12:43:27 ON 27 AUG 2007
E "PMCOL"/CN 25

FILE 'REGISTRY' ENTERED AT 12:44:06 ON 27 AUG 2007
L6 1 S 950-99-2/RN
SET NOTICE 1 DISPLAY
SET NOTICE LOGIN DISPLAY

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 12:44:38 ON 27 AUG 2007
L7 510 S L6
L8 22 S L7 AND (CANCER OR TUMOR)

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 152.10 | 306.03 |

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL

| | ENTRY | SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | -7.02 | -8.58 |

STN INTERNATIONAL LOGOFF AT 13:00:16 ON 27 AUG 2007